MicroED structure of Aeropyrum pernix protoglobin

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Microcrystal electron diffraction (MicroED) is an emerging technique which have shown great potential in solving new and important chemical and biological molecular structures. Several novel structures of small molecules, natural products and peptides have been determined by MicroED using ab initio methods. For protein crystallography, molecular replacement is the most commonly used method to determine new structures, using phase information of a homology model. However, there are so far only a few examples of novel protein structures derived by MicroED. Taking advantage of recent technological advances including higher acceleration voltage and using a highly sensitive camera in counting mode, we have determined the structure of the Aeropyrum pernix protoglobin (ApePgb) variant GLVRSQL.(1) This is an engineered variant of ApePgb that was obtained through directed evolution and which can be used for biocatalytic cyclopropanation, N–H insertion, and Si–H insertion reactions. This is the first structure of an ApePgb and hence, no wild-type structure was available as search model. Instead, the structure was phased by molecular replacement using a predicted model. This shows that MicroED now enables investigation of structures that were previously beyond technological reach.

(1)Porter N, Danelius E, Gonen T, Arnold F. Biocatalytic Carbene Transfer Using Diazirines. ChemRxiv. 2022; 10.26434/chemrxiv-2022-9v4j1.